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Exposure to secondhand tobacco smoke and the frailty syndrome in US older adults

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Abstract

Background. Exposure to secondhand tobacco smoke (SHS) is a well-established risk factor for cardiovascular disease and lung cancer in non-smoking adults. However, few studies have focused on the health consequences of exposure to SHS in older adults. This is the first study to assess the association between SHS and the frailty syndrome in the non-smoking older adult population.

Methods. Cross-sectional study among 2059 non-smoking adults aged ≥60 years who participated in the third U.S. National Health and Nutrition Examination Survey and had completed a physical examination. Exposure to SHS was assessed by serum cotinine concentrations and by self-reported data from the home questionnaire. Frailty was ascertained with a slight modification of the Fried criteria. Analyses were performed with logistic regression and adjusted for the main confounders.

Results. The median (interquartile range) concentration of serum cotinine was 0.095 (IQR: 0.035-0.211) ng/mL. The prevalence of frailty was 6.0%. The odds ratios (95% CI) of frailty comparing the second, third and fourth to the lowest quartile of serum cotinine were, respectively, 1.44 (0.67-3.06), 1.46 (0.75-2.85) and 2.51 (1.06-5.95); p value for trend 0.04. An increased frequency of frailty was also observed in participants reporting to live with ≥2 smokers at home (odds ratio: 5.37; 95% CI: 1.13-25.5).

Conclusions. In the US non-smoking older adult population, exposure to SHS was associated with an increased frequency of frailty. More efforts are needed to protect older adults from SHS, especially at home and in other areas not covered by smoke-free regulations.

Key words: Second hand smoke, cotinine, older adults, frailty.

INTRODUCTION

Exposure to secondhand tobacco smoke (SHS) is a well-established risk factor for coronary heart disease[1], lung cancer[1] and stroke[2] in non-smoking adults; there is also suggestive evidence that SHS could increase the risk of asthma and chronic obstructive pulmonary disease.[1] Older adults may be very susceptible to the effects of SHS because of age-related physiologic changes and coexisting health conditions.[3] Moreover, they may be at increased risk of involuntary exposure because they spend most time indoors and they are at higher risk of functional and economic dependency. Despite this, surprisingly, few studies have focused on the health consequences of exposure to SHS in older adults.[4,5]

Frailty, a potentially preventable geriatric syndrome, is characterized by diminished physiologic reserve across multiple organ systems with decreased ability of the old individual to cope with environmental stressors.[6] Frailty has been linked to increased risk for adverse outcomes in older adults, including falls,[7] disability,[8] institutionalization[9] and death.[10,11] Given the high frequency of frailty and its serious health and disability consequences, extensive research is being conducted to identify preventable risk factors and to understand mechanistic pathways.

In this study, we evaluated for the first time the association between SHS and frailty in the non-smoking older adult population using data from the third US National Health and Nutrition Examination Survey (NHANES III).

METHOD

Study participants

NHANES III was a multistage, stratified, clustered probability survey of the US civilian non-institutionalized population, conducted between 1988 and 1994 by the National

Center for Health Statistics. The survey consisted of a household interview and a standardized physical examination performed in a mobile center. We limited our study to 3086 adults ≥60 years who reported "having never smoked ≥100 cigarettes during their entire life" and had completed the physical examination. To ensure that we did not include smokers in the study, we also excluded participants who had serum cotinine concentrations above 10 ng/mL (N=993). Furthermore, we excluded 34 individuals with missing values in potential confounders (education, body mass index [BMI], morbidities or drug treatments), leading to a final analytical sample of 2059 individuals.

The study protocol was approved by the NHANES Institutional Review Board (IRB), and written informed consent was obtained from all participants.

Study variables

Secondhand Tobacco Smoke

Exposure to SHS was assessed by using self-reported data from the home questionnaire and serum cotinine, a specific biomarker of tobacco exposure.[12] Serum cotinine was measured using high performance liquid chromotography/atmospheric pressure chemical ionization tandem mass spectrometry. The limit of detection (LOD) for serum cotinine using this method was 0.05 ng/mL and values under the LOD were replaced by the square root of 2 (0.035 ng/mL). Never smokers who presented serum cotinine concentrations ≥0.035 ng/mL or who self-reported living with at least 1 person who smoked were considered exposed to SHS.

Frailty

Frailty was assessed with a slight modification of the definition developed by Fried and colleagues [9] in the Cardiovascular Health Study (CHS). Individuals meeting ≥3 of the

following 5 criteria were considered as frail: 1) *Weakness*, considered present if the individual answered "some difficulty", "much difficulty" or "unable to do it" to the question "How much difficulty you have lifting or carrying something as heavy as 10 pounds?"; 2) *Exhaustion*, defined as any of these responses "some difficulty", "much difficulty" or "unable to do it" to the question "How much difficulty do you have walking from one room to the other on the same level?"; 3) *Low body weight*, defined as BMI $\leq$18 kg/m^2; 4) *Slow walking speed*, defined as the worse quintile in the eight-foot walking speed test, adjusted for sex and height[13]; 5) *Low physical activity*, considered present in individuals who answered "less active" to the question: "When compared to most men/women of your age, would you say that you are more active, less active or about the same?"

Potential confounders

Questionnaire information included sex, age, education, race/ethnicity, presence of comorbidities and number of drug treatments used. Participants were asked about their previous history of cardiovascular disease (coronary heart disease, stroke congestive heart failure), hypertension, diabetes, osteoarticular disease (osteoporosis, rheumatoid arthritis and osteoarthritis), respiratory disease (asthma, chronic bronchitis or emphysema) and cancer. During the medical examination, blood pressure was measured three times with the participant seated for 5 minutes and using an appropriate sized cuff. Hypertension was defined as self-reported physician diagnosis of high blood pressure or a mean systolic/diastolic blood pressure $\geq$140/90 mm Hg. Finally, weight and height were measured in standardized conditions, and BMI calculated as weight in kg divided by squared height in m.

Statistical analyses

The association between SHS exposure and the presence of frailty was evaluated using logistic regression. Two sets of models were built, one in which serum cotinine was the main independent variable, and one in which exposure to SHS was defined according to the number of smokers at home. In the first set of models (table 2), participants were classified into quartiles of serum cotinine, with the lowest quartile (individuals with cotinine concentrations under the LOD) being the exposure reference. Additionally, ln-transformed cotinine was modeled as a continuous variable and odds ratios comparing the 75^{th} versus the 25^{th} percentiles of its distribution were derived. In the second set of models (table 3), participants were classified into three categories of exposure according to the number of smokers at home (0, 1, $\geq$2). All models were first adjusted for sex and age (model 1), and then further adjusted for education, ethnicity, BMI, morbidity and number of drug treatments (model 2). Additionally, when the number of smokers at home was the main independent variable, a third model (model 3) further adjusting for the number of rooms per household was fitted.

Next, we estimated the association between cotinine concentrations and frequency of each frailty criterion (table 4). Again, two main models that accounted for the previously defined subsets of covariates were fitted.

Finally, to graphically evaluate the dose-response association between serum cotinine concentrations and frailty, serum cotinine concentrations were separately modeled using restricted cubic splines with knots at the 10^{th} (0.035 ng/mL), 50^{th} (0.095 ng/mL) and 90^{th} (0.645 ng/mL) percentile of its distribution. In all analyses, we took sample weights and NHANES survey design into consideration by using the svy commands in Stata 13.

RESULTS

The mean age of the population was 71.3 years and 74% were women. The median (interquartile range) concentration of serum cotinine was 0.095 (IQR: 0.035-0.211) ng/mL. Around 10% of the population lived with at least one smoker. Compared to individuals whose serum cotinine concentration was undetectable, those with detectable cotinine concentrations were more likely to be men, had lower age, lower medicine consumption, were more likely to be non-Hispanic black, and had lower education and greater BMI (table 1). Additionally, never-smokers living with ≥1 smokers at home showed higher serum cotinine concentrations.

Among the study participants, 166 (6.0%) were frail. Frailty was more common among women, those ≥74 years of age, non-Hispanic white and Mexican-American participants, and those with lower education. After multivariate adjustment, the odds ratio (95% confidence interval [CI] of frailty comparing the second, third and fourth quartiles of serum cotinine to the lowest quartile were, respectively, 1.44 (0.67-3.06), 1.46 (0.75-2.85) and 2.51 (1.06-5.95); p value for trend 0.04 (table 2). In spline regression models (figure 1), the dose-response relationship was progressive over the range of serum cotinine concentrations (p value for the nonlinear component=0.11).

An increased frequency of frailty was also observed in participants living with smokers at home. Compared to those who do not live with smokers, the odds ratio (95% CI) of frailty for those living with 1 or ≥2 smokers were, respectively, 1.46 (0.67-3.20) and 6.82 (1.83-25.4); p value for trend <0.01 (table 3). Results were similar after further adjustment for the number of rooms per household: 1.40 (0.58-3.41), 5.37 (1.13-25.5), p value for trend 0.04.

Table 4 shows the association between serum cotinine and the five components of the frailty syndrome. Higher serum cotinine was associated with higher frequency of weakness and with, a marginally significant, increased frequency of exhaustion.

DISCUSSION

In this sample of non-smoking older adults from the US general population, exposure to SHS, as measured using serum cotinine concentrations and self-reported information on the number of smokers at home, was associated with an increased prevalence of frailty. The association was independent of potential confounders such as sex, age, education, ethnicity, BMI, drug treatments or previous history of cardiovascular disease hypertension, diabetes, osteoarticular disease, chronic respiratory disease and cancer.

Worldwide, around 33% of male and 35% of female non-smoking adults were exposed to SHS in 2004.[14] Since then, many nations have passed bans on smoking in public spaces, but still millions of nonsmokers continue to be exposed to SHS in areas not covered by smoke-free regulations, including homes.[15] In the US only, around 14 million of the non-institutionalized, non-smoking adults aged ≥60 years were exposed to SHS during 2007-2008[15]. Moreover, according to the last Tobacco Use Supplement to the Current Population Survey, fewer than half of households with smokers in the US have adopted smoke free home rules[16]. Because a high proportion of adults ≥60 years reside in nursing homes and most countries have no laws regulating smoking in these settings, the magnitude of SHS exposure among older adults is likely to be greater.

Some studies have shown that active smoking can induce muscular damage and sarcopenia in the old age.[17] In line with this finding, results from the Hallym Aging Study indicated that smoking was associated with higher frequency of decreased grip strength in men aged ≥65 years.[18] In cross-sectional analyses, current smoking[19] and

consumption of ≥ 1 pack/day of cigarettes for ≥ 20 years[20] have been linked with an increased prevalence of frailty indicators, while some prospective cohort studies have shown that baseline smoking status is a strong predictor of frailty [21-23] and disability.[24-27]

Since this is the first study to evaluate the association between SHS and frailty, we cannot compare our results with previous findings. However, there is evidence that SHS increases the risk of several diseases that are linked to frailty, including coronary heart disease, stroke and lung cancer.[1,2] Some studies have also linked SHS exposure in older adults with the risk of dementia[28,29,30], cognitive impairment,[31-33] , and worse scores in the mental health dimension of the SF-36 [34]. Among never-smokers, high lifetime SHS exposure at home has been associated with decreased mineral density in both adult men and women,[35] and with increased risk of osteoporosis in postmenopausal women.[36] Finally, in a cross-sectional study based on NHANES 1999-2002, authors found that SHS exposure among nonsmoking older adults was associated with reduced physical function and reduced gait speed.[32] Interestingly, in our study the association with reduced physical function and reduced gait speed was not statistically significant, suggesting that SHS-related frailty was mainly driven through the high frequency of weakness and exhaustion.

This study has several strengths. First, it includes a large sample representative of the US general population aged ≥ 60 years. Second, the availability of serum cotinine, a specific biomarker of tobacco smoke exposure, reduces the possibility of exposure misclassification and allows for evaluating the dose-response relationship between SHS and frailty. And third, the study accounted for numerous covariates, so that residual confounding is likely to be small.

Some limitations of this study should also be acknowledged. First, the lack of prospective information limits reaching firm conclusions on SHS as a risk factor for frailty. Second, because the sample did not include institutionalized individuals, results cannot not be inferred to this population group. Third, we could not account for differences in cotinine metabolism. Because nicotine is primarily inactivated to cotinine by the hepatic enzyme CYP2A6, variations in its activity can modify serum cotinine concentrations. Similarly, there is some evidence that vegetarians and persons with higher intake of certain foods (i.e. almonds, broccoli or garlic) may have falsely high levels of cotinine. However, we are not aware of reasons why the frequency of slower vs. faster nicotine metabolizers, or of those with high vs. low intake of these specific foods, could vary with frailty status. Finally, although cotinine levels correctly assess recent exposure to secondhand smoke, they may not reflect long term exposure and especially past exposure. However, there is evidence that passive smoking is capable of precipitating acute changes in several physiological processes that are central to the pathogenesis of frailty. Specifically, short-term SHS exposure has been associated with increased circulating markers of inflammation (i.e. IL4, IL6 or TNF-α)[37-40]; changes in the immune response with increased white blood, lymphocyte and granulocyte counts[41]; and elevated levels of markers of endothelial disfunction.[42] Additionally, previous research has found that serum cotinine among never-smokers is associated with biomarkers of oxidative stress (i.e. 8-dihydro-2´deoxyguanosine[43]) and with markers of activation of inflammatory and coagulative processes (i.e homocysteine,[44,45] fibrinogen,[39,45] factor VIII [39]), that are known to be elevated in frail individuals.[46-48]

Conclusions

In the US non-smoking older adult population, exposure to SHS was associated with an increased frequency of frailty. More efforts are needed to protect older adults from SHS, especially at home and in other areas not covered by smoke-free regulations.

Figure title: Odds ratios (95% confidence intervals) of frailty according to serum cotinine concentrations based on restricted cubic splines with knots at the 10^{th}, 50^{th} and 90^{th} of its distribution. **Figure legend:** The reference value is set at the 10^{th} percentile of cotinine distribution. Odds ratios are adjusted for education, race/ethnicity, BMI, cardiovascular disease, hypertension, diabetes, osteoarticular disease, chronic respiratory disease, cancer, and number of drug treatments. Lines represent the Odds ratio (thick line) and 95% confidence interval (dotted lines), and vertical bars represent the histogram of cotinine distribution. Data correspond to the US non-smoking older population.

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Contributions: EGE conceived the study, performed the statistical analyses and drafted the manuscript. FRA and ANA drafted and reviewed the manuscript for important intellectual content. EGE and FRA had primary responsibility for the final content.

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